[0019] FIG. **11**B shows the open circuit potential (OCP) of uncoated and NC coated sample substrates.

[0020] FIG. **12** shows a flow chart for in vivo testing to confirm anti-inflamatory properties, osseointegration, and mechanical testing of coatings, in accordance with embodiments.

DETAILED DESCRIPTION

[0021] Total joint replacement and the use of prostheses/implants are rapidly growing due to higher life expectancy and the growing obesity epidemic. However, 10-15% of implants will fail and will need extensive revision surgery mainly due to osteolysis. At this time, there are no drug or treatment strategies specifically approved for prevention or inhibition of periprosthetic osteolysis.

[0022] It was previously unknown whether coating forms of CNPs would exhibit the same catalytic activity described above. One concern was the ability to create a coating which retained the catalytic and radical scavenging properties described above and in the cited references, as previous studies involved CNPs. In contrast, a nanoceria ("NC") coating is provided herein that is formed on a substrate (or on an intermediate layer between the substrate and the coating) and as such, no longer in nanoparticle form. It is shown through experiments described below the NC coatings developed and disclosed retain the catalytic mimetic activities reported for the CNPs. Moreover the NC coatings enhance osseointegration, and reduce overall osteolysis. Both methods and products are disclosed.

[0023] As to the methods, embodiments disclosed include making an implant comprising the steps of obtaining a substrate comprising materials comprised in whole or in part of metal, ceramic, plastic, or a composite; and depositing a nanoceria coating on at least a portion of the substrate, wherein the nanoceria coating has a predetermined surface roughness parameter and a surface cerium 3+/4+ oxidation state ratio such that said nanoceria coating exhibits catalase mimetic activity, superoxide dismutase mimetic activity, or both. In these and other embodiments, the implant is adapted for the prevention or inhibition of osteolysis.

[0024] Embodiments described herein are based on the discovery that a significant cause of arthroplasty failure occurs due to high levels of free radicals, chronic inflammation and osteolysis. Osteolysis is the destruction of bone tissue. This may occur due to chronic inflammation from particles or debris generated through wear, electrochemical dissolution/corrosion, or a combination thereof. The implant coated at least partially thereon with an NC coating is able to reduce the presence of such free radicals and thus overall inflammation and osteolysis. Therefore, a method is also disclosed for reducing degradation of an implant by placing nanoceria in proximity to a bone-implant interface.

[0025] Further embodiments include an implant, or component of an implant, having said NC coating. As used herein, the term "component" refers to a part of an overall implant, bone implant, or other prosthesis. These implants comprise a NC coating on at least a portion thereof. In such an embodiment, the implant comprises at least a substrate on which an NC coating is coated; there may also be an intermediate layer between the coating and the substrate. Also disclosed are embodiments relating to a coating itself, without respect to any substrate or intervening layer upon which the coating may be disposed. The NC coatings of embodiments have various features. Namely, the coating is characterized by nanoceria having a surface cerium 3+/4+ oxidation state ratio such that such that the coating exhibits catalase mimetic activity, superoxide dismutase mimetic activity, or both.

[0026] Because cell attachment and proliferation of macrophage cells (involved in the osteolytic process) were shown to be inversely proportional with increasing roughness of the coating, the coatings disclosed may also have a predetermined surface roughness (described below). Methods for electrdeposition of an NC coating on a substrate are also disclosed. Broadly, a method comprises electrophoretically forming the coating on a given substrate using a dispersion of CNPs, preferably where the substrate is placed between two counter electrodes (for a total of three electrodes). However, a two electrode setup may also be used. This coating method uses CNPs having surface cerium in the 3+ oxidation state or 4+ oxidation state, or both, and results in an NC coating which has a given 3+/4+ ratio such that the desired and above described anti-inflammatory properties are exhibited. Coatings with both oxidation states are preferable, but either oxidation state imparts advantagous benefits.

[0027] According to another embodiment, a method is provided for conducting an orthopedic procedure in a subject in need thereof. The method involves obtaining an implant having an NC coating as described herein and implanting the implant into the subject at a site of need. The implantation involves positioning the implant so as to have contact with bone tissue. In a specific embodiment, the orthopedic procedure is an arthroplasty procedure, and the implant is one for insertion in or between a joint. Examples of arthroplasty implants include hip replacement implants, knee replacement implants, shoulder replacement, and intervertebral implants. Other related orthopedic implants that may be coated and used in accordance with the embodiments described herein include, but are not limited, plates, screws, rods, cages, dowels and the like used in orthopedic surgeries. A subject as used herein refers to a mammal including but not limited to a human, dog, cat, horse, goat, cow etc. A subject in need is one who has an injury, defect or disease of the musculoskeletal system requiring an orthopedic surgery.

[0028] Furthermore, based on the discoveries herein, an alternative embodiment relates to a bone paste composition that includes CNPs comprising catalase activity, superoxide dismutase activity, or both, and at least one osteoinductive or osteoconductive component. Examples of osteoinductive or osteoconductive components include, but are not limited to, demineralized bone powder as described in U.S. Pat. No. 5,073,373 the contents of which are incorporated herein by reference, collagen, insoluble collagen derivatives, hydroxyapatite, ceramic, calcium phosphate, dicalcium phosphate, tricalcium phosphate, bone morphogentic protein, transforming growth factor (TGF-beta), insulin-like growth factor (IGF-1) (IGF-2), platelet derived growth factor (PDGF), fibroblast growth factors (FGF), vascular endothelial growth factor (VEGF), angiogenic agents, bone promoters, cytokines, interleukins, genetic material, genes encoding bone promoting action, cells containing genes encoding bone promoting action; growth hormones such as somatotropin; bone digestors; antitumor agents; fibronectin; cellular attractants and attachment agents. U.S. Pat. No. 6,695,882, incorporated by reference, teaches other osteoinductive and osteoconductive components.